General

Guideline Title

WHO recommendations for the prevention and treatment of postpartum haemorrhage.

Bibliographic Source(s)

World Health Organization (WHO). WHO recommendations for the prevention and treatment of postpartum haemorrhage. Geneva (Switzerland): World Health Organization (WHO); 2012. 41 p.

Guideline Status

This is the current release of the guideline.

World Health Organization (WHO). WHO recommendations for the prevention of postpartum haemorrhage. Geneva, Switzerland: World Health Organization (WHO); 2007. 116 p.

Recommendations

Major Recommendations

The rating schemes for the quality of the evidence (very low, low, moderate, high) and the strength of the recommendations (weak, strong) are defined at the end of the "Major Recommendations" field.

Recommendations for the Prevention of Postpartum Haemorrhage (PPH) – Uterotonics

1. The use of uterotonics for the prevention of PPH during the third stage of labour is recommended for all births. (Strong recommendation, moderate-quality evidence)
2. Oxytocin (10 IU, intravenous [IV]/intramuscular [IM]) is the recommended uterotonic drug for the prevention of PPH. (Strong recommendation, moderate-quality evidence)
3. In settings where oxytocin is unavailable, the use of other injectable uterotonics (e.g. ergometrine/methylergometrine or the fixed drug combination of oxytocin and ergometrine) or oral misoprostol (600 µg) is recommended. (Strong recommendation, moderate-quality evidence)
4. In settings where skilled birth attendants are not present and oxytocin is unavailable, the administration of misoprostol (600 µg orally [PO]) by community health care workers and lay health workers is recommended for the prevention of PPH. (Strong recommendation, moderate-quality evidence)

Remarks

- Available comparisons are limited, but a significant difference between the benefits of oxytocin and ergometrine is unlikely. These recommendations place a high value on avoiding the adverse effects of ergometrine and assume a similar benefit from using oxytocin and

ergometrine for the prevention of PPH.

- Caution should be exercised when opting for ergot derivatives for the prevention of PPH as these drugs have clear contraindications in women with hypertensive disorders. Thus, it is probably safer to avoid the use of ergot derivatives in unscreened populations.
- Misoprostol (600 μg PO) was regarded by the guideline development group (GDG) as an effective drug for the prevention of PPH. However, the GDG considered the relative benefits of oxytocin compared to misoprostol in preventing blood loss, as well as the increased adverse effects of misoprostol compared to oxytocin. The GDG acknowledged that there is no evidence to show that a 600 μg dose of misoprostol provides greater efficacy over a 400 μg dose. Lower doses have a lower side-effect profile but the efficacy of lower doses of misoprostol has not been evaluated sufficiently.
- The recommendations concerning alternative uterotonics should not detract from the objective of making oxytocin as widely accessible as possible.
- In view of past concerns regarding the community-level distribution of misoprostol and the potential for serious consequences of administration before birth, the GDG places emphasis on training persons administering misoprostol and monitoring community distribution interventions with scientifically sound methods and appropriate indicators.

Recommendations for the Prevention of PPH – Cord Management and Uterine Massage

5. In settings where skilled birth attendants are available, controlled cord traction (CCT) is recommended for vaginal births if the care provider and the parturient woman regard a small reduction in blood loss and a small reduction in the duration of the third stage of labour as important. (Weak recommendation, high-quality evidence)
6. In settings where skilled birth attendants are unavailable, CCT is not recommended. (Strong recommendation, moderate-quality evidence)
7. Late cord clamping (performed approximately 1 to 3 minutes after birth) is recommended for all births while initiating simultaneous essential newborn care. (Strong recommendation, moderate-quality evidence)
8. Early cord clamping (<1 minute after birth) is not recommended unless the neonate is asphyxiated and needs to be moved immediately for resuscitation. (Strong recommendation, moderateâ€'quality evidence)
9. Sustained uterine massage is not recommended as an intervention to prevent PPH in women who have received prophylactic oxytocin. (Weak recommendation, low-quality evidence)
10. Postpartum abdominal uterine tonus assessment for early identification of uterine atony is recommended for all women. (Strong recommendation, very-low-quality evidence)

Remarks

- Recommendations 5 and 6 are based on a large randomised controlled trial (RCT) in which oxytocin 10 IU was used for the prevention of PPH in all participants. Based on this evidence, CCT was regarded as safe when applied by skilled birth attendants as it provides small beneficial effects on blood loss (average reduction of 11 ml on blood loss) and on the duration of the third stage of labour (average reduction of 6 minutes). The decision to implement CCT in the context of a prophylactic uterotonic drug should be discussed by the care provider and the woman herself.
- If ergot alkaloids are used for the prevention of PPH, then CCT to minimize placenta retention is regarded as essential.
- There is insufficient evidence to determine the benefit or risk of CCT when used in conjunction with misoprostol.
- CCT is the first intervention to treat retained placenta, therefore the teaching of CCT in medical and midwifery curricula is essential.
- The evidence base for recommendations for the timing of cord clamping includes both vaginal and caesarean births. The GDG considers this recommendation to be equally important for caesarean sections.
- Delayed clamping should be performed during the provision of essential newborn care. For essential newborn care and resuscitation, please refer to the WHO guidelines on neonatal resuscitation.
- The recommendations for the timing of cord clamping apply equally to preterm and term births. The GDG considers the benefits of delayed clamping for preterm infants to be particularly important.
- Some health professionals working in areas of high human immunodeficiency virus (HIV) prevalence have expressed concern regarding delayed cord clamping as part of management of the third stage of labour. These professionals are concerned that during placental separation, a partially detached placenta could be exposed to maternal blood and this could lead to a micro-transfusion of maternal blood to the baby. It has been demonstrated that the potential for maternal-to-child transmission of HIV can take place at three different points in time: micro-transfusions of maternal blood to the fetus during pregnancy (intra-uterine HIV transmission), exposure to maternal blood and vaginal secretions when the fetus passes through the birth canal in vaginal deliveries (intra-partum transmission), and during breastfeeding (postnatal infection). For this reason, the main intervention to reduce the maternal-to-child transmission is the reduction of maternal viral load through the use of antiretroviral drugs during pregnancy, childbirth and postnatal period. There is no evidence that delaying the cord clamping increases the possibility of HIV transmission from the mother to the newborn. Maternal blood percolates through the placental intervillous space throughout pregnancy with a relatively low risk of maternal fetal transmission before delivery. It is highly unlikely that separation of the placenta increases exposure to maternal blood, and is highly unlikely that it disrupts the fetal placental circulation (i.e., it is

unlikely that during placenta separation the newborn circulation is exposed to maternal blood). Thus, the proven benefits of a 1 to 3 minute delay at least in clamping the cord outweigh the theoretical, and unproven, harms. Late cord clamping is recommended even among women living with HIV or women with unknown HIV status.

- There is a lack of evidence regarding the role of uterine massage for PPH prevention when no uterotonic drugs are used, or if a uterotonic drug other than oxytocin is used.
- Although the GDG acknowledged that one small study reported that sustained uterine massage and clot expulsion were associated with a reduction in the use of additional uterotonics, there is lack of robust evidence supporting other benefits. However, the GDG considered that routine and frequent uterine tone assessment remains a crucial part of immediate postpartum care, particularly for the optimization of early PPH diagnosis.
- Based on the most recent evidence, understanding of the contribution of each component of the active management of the third stage of labour package has evolved. The GDG considered that this package has a primary intervention: the use of an uterotonic. In the context of oxytocin use, CCT may add a small benefit, while uterine massage may add no benefit for the prevention of PPH. Early cord clamping is generally contraindicated.

Recommendations for the Prevention of PPH in Caesarean Sections

11. Oxytocin (IV or IM) is the recommended uterotonic drug for the prevention of PPH in caesarean section. (Strong recommendation, moderate-quality evidence)
12. Cord traction is the recommended method for the removal of the placenta in caesarean section. (Strong recommendation, moderate-quality evidence)

Remarks

- The GDG noted that, in terms of blood loss, there was not enough evidence to recommend oxytocin infusion over IV bolus injection. However, due to concerns regarding adverse haemodynamic effects, the GDG considered that if an IV bolus injection is used, a slow injection rate is preferred and a rapid injection rate should be avoided.
- The GDG noted that the combination of an oxytocin infusion after an initial IV bolus of oxytocin after caesarean delivery reduces the need for additional uterotonic agents but does not affect the overall occurrence of major obstetric haemorrhage.
- The GDG noted that carbetocin is associated with a reduction in the use of additional uterotonic agents but with no difference in the occurrence of major obstetric haemorrhage. In addition, the GDG noted that the use of carbetocin is considerably more expensive than oxytocin. This remark is equally applicable to vaginal deliveries.

Recommendations for the Treatment of PPH – Uterotonics

13. Intravenous oxytocin is the recommended uterotonic drug for the treatment of PPH. (Strong recommendation, moderate quality evidence)
14. If intravenous oxytocin is unavailable, or if the bleeding does not respond to oxytocin, the use of intravenous ergometrine, oxytocin-ergometrine fixed dose, or a prostaglandin drug (including sublingual misoprostol, 800 μg) is recommended. (Strong recommendation, low-quality evidence)

Remarks

- The GDG recommended IV oxytocin as the first line uterotonic drug for the treatment of PPH, including when women have already received this drug for the prophylaxis of PPH.
- The GDG recognized that IV oxytocin may not be available in all settings. It encourages health care decision-makers in these settings to strive to make oxytocin available.
- In settings where IV oxytocin is unavailable to women who have received prophylactic IM oxytocin during the third stage of labour, the GDG considered misoprostol to be a valid alternative.
- If PPH prophylaxis with misoprostol has been administered and if injectable uterotonics are unavailable, there is insufficient evidence to guide further misoprostol dosing and consideration must be given to the risk of potential toxicity.
- There is no added benefit to offering misoprostol simultaneously to women receiving oxytocin for the treatment of PPH (i.e., adjunct misoprostol).
- The GDG noted that the two largest trials of misoprostol for the treatment of PPH reported the use of a 800 μg dose administered sublingually. The majority of the GDG members agreed that 800 μg is an acceptable sublingual misoprostol dose for the treatment of PPH, though some members of the GDG expressed concern related to the risk of hyperpyrexia associated with this dosage.
- If IV oxytocin has been used for the treatment of PPH and the bleeding does not stop, there is a paucity of data to recommend preferences for second line uterotonic drug treatment. Decisions in such situations must be guided by the experience of the provider, the availability of the drugs, and by known contraindications.

- In situations in which IM oxytocin can be administered and there is no possibility of IV treatment with ergot alkaloids/injectable prostaglandins, there is a paucity of data to recommend a preference of IM oxytocin over misoprostol or other uterotonics. Decisions in such situations must be guided by the experience of the provider, the availability of the drugs, and by known contraindications.

Recommendations for the Treatment of PPH – Fluid Resuscitation and Tranexamic Acid

15. The use of isotonic crystalloids is recommended in preference to the use of colloids for the intravenous fluid resuscitation of women with PPH. (Strong recommendation, low-quality evidence)
16. The use of tranexamic acid is recommended for the treatment of PPH if oxytocin and other uterotonics fail to stop the bleeding or if it is thought that the bleeding may be partly due to trauma. (Weak recommendation, moderate-quality evidence)

Remarks

- Evidence for the recommendation of tranexamic acid was extrapolated from the literature on surgery and trauma, which shows tranexamic acid to be a safe option for the treatment of trauma-related bleeding.

Recommendations for the Treatment of PPH – Manoeuvres and Other Procedures

17. Uterine massage is recommended for the treatment of PPH. (Strong recommendation, very low-quality evidence)
18. If women do not respond to treatment using uterotonics, or if uterotonics are unavailable, the use of intrauterine balloon tamponade is recommended for the treatment of PPH due to uterine atony. (Weak recommendation, very-low-quality evidence)
19. If other measures have failed and if the necessary resources are available, the use of uterine artery embolization is recommended as a treatment for PPH due to uterine atony. (Weak recommendation, very-low-quality evidence)
20. If bleeding does not stop in spite of treatment using uterotonics and other available conservative interventions (e.g., uterine massage, balloon tamponade), the use of surgical interventions is recommended. (Strong recommendation, very-low-quality evidence)
21. The use of bimanual uterine compression is recommended as a temporizing measure until appropriate care is available for the treatment of PPH due to uterine atony after vaginal delivery. (Weak recommendation, very-low-quality evidence)
22. The use of external aortic compression for the treatment of PPH due to uterine atony after vaginal birth is recommended as a temporizing measure until appropriate care is available. (Weak recommendation, very-low-quality evidence)
23. The use of non-pneumatic anti-shock garments is recommended as a temporizing measure until appropriate care is available. (Weak recommendation, low-quality evidence)
24. The use of uterine packing is not recommended for the treatment of PPH due to uterine atony after vaginal birth. (Weak recommendation, very-low-quality evidence)

Remarks

- The GDG noted that the application of these interventions requires training and that maternal discomfort and complications associated with these procedures have been reported.
- Uterine massage as a therapeutic measure is defined as the rubbing of the uterus achieved through the manual massaging of the abdomen. This is typically sustained until the bleeding stops or the uterus contracts. The GDP considered that uterine massage should be started once PPH has been diagnosed.
- The initial rubbing of the uterus and expression of blood clots are not regarded as therapeutic uterine massage.
- When rating the recommendation #17 as 'strong', the low cost and safety of uterine massage were taken into account.
- The use of balloon tamponade was considered by the GDG to be a measure that can potentially avoid surgery or as a temporizing measure while awaiting transfer to a higher level facility. The GDG acknowledges that balloon tamponade can be obtained with specific devices as well as with lower cost adaptations, including those based on the use of condoms and surgical gloves.
- The GDG noted that uterine artery embolization requires significant resources, in terms of the cost of the treatment, the facilities, and the training of health care workers.
- The GDG noted that conservative surgical approaches should be tried first. If these do not work, they should be followed by more invasive procedures. Compression sutures, for example, may be attempted as a first intervention, and if these fail, then uterine, utero-ovarian and hypogastric vessel ligation may be tried. If life-threatening bleeding continues even after ligation, then a subtotal (otherwise known as supracervical) or total hysterectomy should be performed.
- The GDG acknowledged that the level of health care provider skills will play a role in the selection and sequence of the surgical interventions.
- External aortic compression has long been recommended as a potential life-saving technique, and mechanical compression of the aorta, if successful, slows blood loss. The GDG placed a high value on this procedure as a temporizing measure in the treatment of PPH.
- The GDG noted that research evaluating the potential benefits and harms of non-pneumatic anti-shock garments is ongoing. Based on the

evidence available, the GDG regarded non-pneumatic anti-shock garments as a temporizing measure while transfer is awaited.
- The GDG noted that there was no evidence of benefit of uterine packing and placed a high value on concerns regarding its potential harm.

Recommendations for the Treatment of Retained Placenta

25. If the placenta is not expelled spontaneously, the use of additional oxytocin (10 IU, IV/IM) in combination with controlled cord traction is recommended. (Weak recommendation, very low-quality evidence)
26. The use of ergometrine for the management of a retained placenta is not recommended as this may cause tetanic uterine contractions which may delay the expulsion of the placenta. (Weak recommendation, very-low-quality evidence)
27. The use of prostaglandin E2 alpha (dinoprostone or sulprostone) in the management of retained placenta is not recommended. (Weak recommendation, very-low-quality evidence)
28. A single dose of antibiotics (ampicillin or first-generation cephalosporin) is recommended if manual removal of the placenta is practised. (Weak recommendation, very-low-quality evidence)

Remarks

- The GDG found no empirical evidence to support recommending the use of uterotonics for the management of a retained placenta in the absence of haemorrhage. The above recommendation was reached by consensus.
- The WHO guide *Managing complications in pregnancy and childbirth* states that if a placenta is not expelled within 30 minutes after the delivery of a baby, the woman should be diagnosed as having a retained placenta. Since there is no evidence for or against this definition, the delay used before this condition is diagnosed is left to the judgement of the clinician.
- The same WHO guide also suggests that in the absence of haemorrhage, the woman should be observed for a further 30 minutes after the initial 30 minutes, before the manual removal of the placenta is attempted. The GDG noted that spontaneous expulsion of the placenta can still occur, even in the absence of bleeding. A conservative approach is therefore advised and the timing of the manual removal of the placenta as a definitive treatment is left to the judgement of the clinician.
- The recommendation regarding the use of prostaglandin E2 is informed by a lack of evidence on this question and also by concerns related to adverse events, particularly cardiac events.
- Direct evidence of the value of antibiotic prophylaxis after the manual removal of the placenta was not available. The GDG considered indirect evidence of the benefit of prophylactic antibiotics from studies of caesarean section and abortion, as well as observational studies of other intrauterine manipulations.
- Current practice suggests that ampicillin or first-generation cephalosporins may be administered when the manual removal of the placenta is performed.
- This question was identified as a research priority for settings in which prophylactic antibiotics are not routinely administered and those with low infectious morbidity.

Health Systems and Organization of Care Recommendations for the Prevention and Treatment of PPH

29. The use of formal protocols by health facilities for the prevention and treatment of PPH is recommended. (Weak recommendation, moderate-quality evidence)
30. The use of formal protocols for referral of women to a higher level of care is recommended for health facilities. (Weak recommendation, very-low-quality evidence)
31. The use of simulations of PPH treatment is recommended for pre-service and in-service training programmes. (Weak recommendation, very-low-quality evidence)
32. Monitoring the use of uterotonics after birth for the prevention of PPH is recommended as a process indicator for programmatic evaluation. (Weak recommendation, very-low-quality evidence)

Remarks

- Routine and frequent uterine tone assessment remains a crucial part of immediate postpartum care, particularly for optimizing the early diagnosis of PPH.
- The GDG acknowledged that the implementation of formal protocols is a complex process which will require the local adaptation of general guidelines.
- The GDG placed a high value on the costs of simulation programmes and acknowledged that there are different types of simulation programmes. Some programmes are hi-tech, computerized and costly while others are less expensive and more likely to be affordable in low- and middle-income countries. The GDG identified improvement in communication between health care providers and patients and their family members as an important priority in the training of health care providers in PPH management.
- The GDG recommended monitoring the use of prophylactic uterotonics. This recommendation is based on experience from other areas of

health care, particularly child health, where content-based health indicators are common and regarded as useful for programmatic purposes. The suggested indicator is calculated as the number of women receiving prophylactic uterotonic drugs after birth divided by all women giving birth.

Statements Related to Topics for Which There Is Insufficient Evidence to Issue a Recommendation

A. There is insufficient evidence to recommend one oxytocin route over another for the prevention of PPH.
B. There is insufficient evidence to recommend the use of recombinant factor VIIa for the treatment of PPH.
C. There is insufficient evidence to recommend the use of intraumbilical vein injection of oxytocin as a treatment for retained placenta.
D. There is insufficient evidence to recommend the antenatal distribution of misoprostol to pregnant women for self-administration for the prevention of PPH.
E. There is insufficient evidence to recommend the measurement of blood loss over clinical estimation of blood loss.

Remarks

- The GDG noted that there are three ongoing trials in which the IV and IM routes for oxytocin administration are being compared for the prevention of PPH.
- The GDG considered there to be insufficient evidence to recommend the use of oxytocin infusion over IV bolus injection with regard to blood loss. However, in light of concerns about the potential adverse haemodynamic effects, the GDG considered that if IV bolus injection treatment is to be used then a slow injection rate is preferred and a rapid injection rate should be avoided.
- In the context of PPH, the GDP considered that the use of recombinant factor VIIa should be limited to women with specific haematological indications. The group regarded the recombinant factor VIIa as a potentially life-saving drug, but noted that it is also associated with life-threatening side-effects. Moreover, recombinant factor VIIa is expensive and may be difficult to administer.
- The GDG acknowledged that while there is a paucity of data to recommend intraumbilical vein injection of oxytocin as a treatment for retained placenta, the procedure itself has not been shown to cause harm and demonstrates a non-significant trend towards a lower risk of requiring the manual removal of the placenta.
- The GDG acknowledged that a number of countries have embarked on community-level programmes of misoprostol distribution and considered that this should be done in the context of research (where reliable data on coverage, safety and health outcomes can be collected).
- The GDG noted that all trials included in the systematic review on the measurement of blood loss were conducted in developed countries and views the applicability of this evidence to low- and middle-income countries as very uncertain.

Definitions:

Significance of the Four Levels of Evidence

Quality	Definition	Implications
High	The guideline development group is very confident that the true effect lies close to that of the estimate of the effect	Further research is very unlikely to change confidence in the estimate of effect
Moderate	The guideline development group is moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate
Low	Confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the true effect	Further research is very likely to have an important impact on confidence in the estimate of effect and is unlikely to change the estimate
Very low	The group has very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect	Any estimate of effect is very uncertain

Strength of the Recommendations

The strength of the recommendations discussed was aligned initially with the quality of the evidence (i.e., at the start of the discussion, strong recommendations were based on evidence of 'moderate' and 'high' quality, while weak recommendations were based on evidence of 'low' and 'very low' quality). In addition to the quality of the evidence, the following factors were considered when determining the final recommendation and its strength: values and preferences, the magnitude of effect, the balance of benefits versus disadvantages, resource usage, and feasibility.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Postpartum haemorrhage (PPH)

Guideline Category

Management

Prevention

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Nursing

Obstetrics and Gynecology

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Hospitals

Nurses

Physician Assistants

Physicians

Public Health Departments

Guideline Objective(s)

- To revise previous World Health Organization (WHO) recommendations for the prevention and treatment of postpartum haemorrhage (PPH) and to add new recommendations
- To provide a foundation for the implementation of strategic policy and programme developments for interventions shown to have been effective in reducing the burden of PPH

Target Population

- All women giving birth either vaginally or by caesarean section (*prevention*)
- Women with postpartum haemorrhage (*treatment*)

Interventions and Practices Considered

Prevention

1. Active management of the third stage of labor by skilled attendants to all women
2. Uterotonic drugs
    - Oxytocin
    - Ergometrine/methylergometrine
    - Fixed drug combination of oxytocin and ergometrine
    - Misoprostol
3. Controlled cord traction
4. Late cord clamping
5. Sustained uterine massage (not recommended following oxytocin administration)
6. Postpartum abdominal uterine tonus assessment
7. Prevention of post-partum haemorrhage in caesarean sections (oxytocin, controlled cord traction)

Treatment/Management

1. Intravenous oxytocin
2. Intravenous ergometrine
3. Oxytocin-ergometrine fixed dose
4. Prostaglandin drug (including sublingual misoprostol)
5. Isotonic crystalloids for initial intravenous fluid resuscitation
6. Tranexamic acid
7. Uterine massage
8. Intrauterine balloon tamponade
9. Uterine artery embolization
10. Surgical interventions
11. Bimanual uterine compression
12. External aortic compression
13. Non-pneumatic anti-shock garments
14. Oxytocin in combination with controlled cord traction
15. Antibiotics (ampicillin or first-generation cephalosporin)
16. Organization of care
    - Use of formal protocols by health facilities for the prevention and treatment of postpartum haemorrhage (PPH)
    - Use of formal protocols for referral of women to a higher level of care
    - Use of simulations of PPH treatment for pre-service and in-service training programmes
    - Monitoring the use of uterotonics after birth for the prevention of PPH

Note: The following were considered but not recommended: uterine packing and ergotamine or prostaglandin E2 for retained placenta.

Major Outcomes Considered

- Maternal mortality
- Maternal morbidity

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Cochrane systematic reviews of randomized controlled trials (RCTs) were the primary source of evidence for the recommendations. Using the assembled list of questions and outcomes, the guideline steering group identified Cochrane systematic reviews that were either relevant or potentially relevant and then evaluated whether any needed updating. A review was considered to be outdated if the last specified date for new trial searches was two years ago or more, or if there were relevant studies still awaiting assessment, as identified by the standard search procedures of the Cochrane Pregnancy and Childbirth Group. Updates were performed using specific standard search strategies. The corresponding authors of the outdated reviews were invited to update them within a specified time period. In instances in which the corresponding authors were unable to do so, the updates were undertaken by members of the guideline steering group. The search strategies employed to identify the trials and the specific criteria for trial inclusion and exclusion are described in the individual systematic reviews. A systematic review of literature that included non-randomized trials was carried out by the guideline steering group members when randomized-trial data related to specific questions were scarce.

Number of Source Documents

The recommendations included in this guideline are based on a total of 22 Cochrane systematic reviews.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Significance of the Four Levels of Evidence

Quality	Definition	Implications
High	The guideline development group is very confident that the true effect lies close to that of the estimate of the effect	Further research is very unlikely to change confidence in the estimate of effect
Moderate	The guideline development group is moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate
Low	Confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the true effect	Further research is very likely to have an important impact on confidence in the estimate of effect and is unlikely to change the estimate
Very low	The group has very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect	Any estimate of effect is very uncertain

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The following procedures were used to extract the evidence for this guideline from each of the systematic reviews: first, the most recent version of the Review Manager (RevMan) file was retrieved from the Cochrane Pregnancy and Childbirth Cochrane Group and customized to reflect the key

comparisons and outcomes (those that were not relevant to the guideline were excluded). Then the RevMan file was exported to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) profiler software and GRADE criteria were used to critically appraise the retrieved scientific evidence. Finally, evidence profiles (in the form of GRADE tables) were prepared for each comparison. An online content management system developed for the Guideline development, Research priorities, Evidence synthesis, Applicability of evidence, Transfer of knowledge (GREAT) project, namely the Guideline Production System, was used to handle and share electronic files.

The evidence presented in the GRADE tables was derived from a larger body of data extracted primarily from Cochrane reviews which, in many cases, contained multiple comparisons (Evidence Base [EB] Tables 1 to 70). Each GRADE table relates to one specific question or comparison, but some GRADE tables do not contain data for all critical outcomes. This is because data for those outcomes were not available in the Cochrane reviews. The raw data which constitute the basis of the GRADE tables are not included in this document, but readers interested in how these GRADE tables were constructed may request access to this information. The guideline steering group used the information presented in the GRADE tables to check if any existing recommendations (included in the 2007 or 2009 documents) needed to be revised, and to draft recommendations that related to the new questions. Each recommendation was allocated to a thematic module which included the narrative summaries of evidence and the relevant GRADE tables. The standardized criteria used in grading the evidence and the thematic modules (including the GRADE tables) are not included in the guideline document. They have been published separately online in a document entitled *WHO recommendations for preventing and treating PPH: evidence base* (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Balance Sheets

Expert Consensus (Consensus Development Conference)

Description of Methods Used to Formulate the Recommendations

This guideline is an update of the *WHO recommendations for the prevention of postpartum haemorrhage (PPH)* published in 2007 and the *WHO guidelines for the management of PPH and retained placenta* published in 2009. This document represents the World Health Organization (WHO)'s normative support for using evidence-informed policies and practices in all countries. The guideline forms part of a WHO knowledge-to-action project entitled GREAT (Guideline development, Research priorities, Evidence synthesis, Applicability of evidence, Transfer of knowledge) and was developed using standardized operating procedures in accordance with the process described in the "WHO handbook for guideline development" (see the "Availability of Companion Documents" field). In summary, the process included: (i) the identification of critical questions and critical outcomes, (ii) the retrieval of the evidence, (iii) the assessment and synthesis of evidence, (iv) the formulation of recommendations, and (v) planning for the dissemination, implementation, impact evaluation and updating of the guideline.

Two technical groups have worked in the development of this guideline. A small operative group composed of staff from the WHO's Department of Reproductive Health and Research, and Department of Maternal, Newborn, Child and Adolescent Health (MCA), as well as two external experts and a larger group with international stakeholders including midwives, obstetricians, neonatologists, researchers, experts in research synthesis, experts in health care programmes, and consumer representatives (the Guideline Development Group – GDG). The guideline steering group was formed in the very beginning of the project and reviewed the previous WHO guidelines on prevention and treatment of PPH. This group prepared a list of potential additional questions related to the prevention and treatment of PPH. Next, the GDG reviewed and prioritized the draft questions. The guideline steering group then produced a list of all the questions to be addressed. This included both questions from the earlier versions of the guideline as well as new ones. The guideline steering group also adopted the outcomes used in the 2007 and 2009 guideline documents. These outcomes, as before, were rated on a scale from 1 to 9. A question or outcome was defined as 'critical' if it was given an average score of 7 or more. Questions and outcomes with a score of between 4 and 6 were considered 'important but not critical', while those with a score lower than 4 were not considered to be important for the purposes of the guideline (see Annex 2 of the original guideline document).

A preliminary online consultation was held to review the draft recommendations. The draft recommendations and supporting evidence were made available to a large number of international stakeholders who were then asked to respond to an online survey. In addition, the preliminary online consultation identified other previous recommendations that needed to be discussed at the WHO Technical Consultation on the Prevention and Treatment of PPH held in Montreux, Switzerland, 6–8 March 2012. A subset of the international group of experts (who had participated in the online consultations) and other additional experts were invited to attend the Technical Consultation (see Annex 1 of the original guideline document for a full list of participants). The draft recommendations, the narrative summaries of evidence, the GRADE tables for the new and previous recommendations, and other related documents were provided in advance to participants. Balance worksheets were used during the Technical Consultation to summarize the values, preferences and judgements made about the strength of the new and revised recommendations.

Decision-making during the Technical Consultation

At the beginning of the Technical Consultation, the participants discussed and adopted a list of recommendations which needed to be addressed during the meeting. This included the new recommendations as well as previous recommendations that needed to be reviewed and possibly revised. The following protocol was used for the Technical Consultation: the meeting was structured to allow participants to discuss the proposed list of recommendations and these recommendations were revised, as needed, through group discussion. The final adoption of each recommendation was made by consensus – defined as the agreement by three quarters or more of the participants – provided that those who disagreed did not feel strongly about their position. Strong disagreements were recorded as such in the guideline. If the participants were unable to reach a consensus, the disputed recommendation, or any other decision, was put to a vote. A recommendation or decision stood if a simple majority (more than half of the participants) voted in support of it, unless the disagreement related to a safety concern, in which case the WHO Secretariat would choose not to issue a recommendation at all. WHO staff attending the meeting, external technical experts involved in the collection and grading of the evidence, and observers were not eligible to vote. In addition to discussing the scientific evidence and its quality, relevant applicability issues, costs and other judgements were also taken into consideration when formulating the final recommendations.

Rating Scheme for the Strength of the Recommendations

The strength of the recommendations discussed was aligned initially with the quality of the evidence (i.e., at the start of the discussion, strong recommendations were based on evidence of 'moderate' and 'high' quality, while weak recommendations were based on evidence of 'low' and 'very low' quality). In addition to the quality of the evidence, the following factors were considered when determining the final recommendation and its strength: values and preferences, the magnitude of effect, the balance of benefits versus disadvantages, resource usage, and feasibility.

Cost Analysis

The guideline developers reviewed a published cost analysis.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Prior to the Technical Consultation, the guideline steering group prepared a preliminary version of this document using a guideline reporting template which had been developed as part of the World Health Organization's Guideline development, Research priorities, Evidence synthesis, Applicability of evidence, Transfer of knowledge (GREAT) project. The draft guideline was reviewed by Technical Consultation participants at the meeting in Montreux. During the meeting, the draft guideline was modified in line with participant deliberation and comments. Feedback received during the preliminary online consultation was also discussed and incorporated into the document where appropriate. After the meeting, members of the guideline steering group worked to ensure that a revised version of the document accurately reflected the deliberations and decisions of the participants. The revised draft guideline document was sent to two external peer reviewers and their inputs were carefully evaluated by the guideline steering group and document revisions made accordingly. The guideline steering group refrained from making substantive changes after the meeting in Montreux to the guideline scoping (such as the further expansion of the guideline scoping) or to the recommendations. The revised version was returned electronically to those who had attended the Technical Consultation for their approval.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate treatment of postpartum hemorrhage, and management of the third stage of labor to prevent postpartum hemorrhage

Potential Harms

Side effects of uterotonic drugs, including nausea, vomiting, diarrhoea, hypertension, shivering, and temperatures over 38 degrees C

Contraindications

Contraindications

- Controlled cord traction (CCT) is now regarded as optional in settings where skilled birth attendants are available, and is contraindicated in settings where skilled attendants do not assist with births.
- Early cord clamping is generally contraindicated.
- Caution should be exercised when opting for ergot derivatives for the prevention of post-partum hemorrhage (PPH) as these drugs have clear contraindications in women with hypertensive disorders.

Qualifying Statements

Qualifying Statements

- The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city, or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.
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- This guideline document is not intended to provide a comprehensive practical guide for the prevention and treatment of postpartum haemorrhage (PPH).

Implementation of the Guideline

Description of Implementation Strategy

Dissemination and Implementation of the Guideline

The ultimate goal of this guideline is to improve the quality of care and health outcomes related to postpartum haemorrhage (PPH). Therefore the dissemination and implementation of this guideline are crucial steps that should be undertaken by the international community and local health care services. The World Health Organization (WHO) Department of Reproductive Health and Research has adopted a formal knowledge-to-action framework for the dissemination, adaptation and implementation of guidelines. In addition to this framework, a list of priority actions was

established during the WHO Technical Consultation which will be used by the WHO and other partners to foster the dissemination and implementation of this guideline:

- Promote discussion, dissemination and uptake during the FIGO (International Federation of Gynecology and Obstetrics) meeting in Rome 2012
- Prepare the translation of WHO Executive Summary: three to five pages into six official United Nations languages
- Prepare guideline derivatives for policy-makers, consumers, clinicians and other groups (e.g., a two-page policy brief, a press release for engaging the public via the media, Managing Complications in Pregnancy and Childbirth update)
- Maximize the dissemination of these guidelines across WHO (regional and country offices)
- Increase the visibility and availability of WHO guidelines
- Prepare WHO–United Nations Population Fund (UNFPA) Joint Statements related to the main recommendations of these guidelines
- Seek endorsement by national and international professional societies, including FIGO, International Confederation of Midwives, and others (e.g., American Congress of Obstetricians and Gynecologists, Royal College of Obstetricians and Gynaecologists)
- Disseminate WHO guidelines in Health Sector Review meetings
- Foster agreement between guidelines (e.g., FIGO) for unified recommendations
- Promote the development of local guidelines/protocols based on these guidelines
- Disseminate these guidelines using WHO guidance community and Knowledge Gateway to virtual community
- Promote active engagement and dialogue rather than passive distribution and action plans
- Foster availability of injectable uterotonics
- Promote the development of tools to facilitate the formulation of health policies based on evidence-based guidelines
- Promote task shifting (including independent use by all care providers skilled in the use of injectable uterotonics).

Guideline Dissemination and Evaluation

The recommendations in this guideline will be disseminated through a broad network of international partners, including WHO country and regional offices, ministries of health, WHO collaborating centres, other United Nations agencies, and non-governmental organizations. They will also be published on the WHO website and in the WHO Reproductive Health Library, where they will be accompanied by an independent critical appraisal based on the AGREE (Appraisal of Guidelines Research and Evaluation) instrument . A policy brief will also be developed for a wide range of policy-makers, programme managers and clinicians, and then disseminated through WHO country offices.

Guideline Implementation

The successful introduction of evidence-based policies related to the prevention and management of PPH into national programmes and health care services depends on well-planned and participatory consensus-driven processes of adaptation and implementation. These processes may include the development or revision of existing national guidelines or protocols based on this document.

The recommendations contained in the original guideline should be adapted into locally-appropriate documents that are able to meet the specific needs of each country and health service. Modifications to the recommendations, where necessary, should be limited to weak recommendations and justifications for any changes made in an explicit and transparent manner.

An enabling environment should be created for the use of these recommendations (for example, by widening the availability of uterotonics), including changes in the behaviour of health care practitioners to enable the use of evidence-based practices. Local professional societies may play important roles in this process and an all-inclusive and participatory process should be encouraged. The WHO's Department of Reproductive Health and Research has published specific guidance on the introduction of the WHO's reproductive health guidelines and tools in national programmes.

Refer to Section 6 of the original guideline document for "Applicability Issues," including anticipated impact on the organization of care and resources and monitoring and evaluating the guideline implementation.

Implementation Tools

Audit Criteria/Indicators

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Staying Healthy

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

World Health Organization (WHO). WHO recommendations for the prevention and treatment of postpartum haemorrhage. Geneva (Switzerland): World Health Organization (WHO); 2012. 41 p.

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2007 (revised 2012)

Guideline Developer(s)

World Health Organization - International Agency

Source(s) of Funding

World Health Organization

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Guideline Development Group

Guideline Steering Group

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Financial Disclosures/Conflicts of Interest

According to World Health Organization (WHO) regulations, all experts must declare their relevant interests prior to participation in WHO

meetings. All guideline development group (GDG) members and participants were therefore required to complete a Declaration of Interest Form before the meeting. These were reviewed by the guideline steering group before the group composition and invitations were finalized. The external advisers also verbally declared potential conflicts of interest at the beginning of the meeting. The procedures for the management of conflicts of interests were undertaken in accordance with the "WHO guidelines for declaration of interests (WHO experts)". In summary, all members of the GDG declared that they had no commercial or financial interests that were directly or indirectly related to the topic of the meeting/guideline. Seven members of the GDG were involved in academic work related to the topic of the guideline, but this involvement was not considered to be a conflict of interest and the full participation of all the selected experts was deemed appropriate. A table summarizing the declarations of interest made by members of the GDG is included in Annex 1 of the original guideline document.

Guideline Status

This is the current release of the guideline.

World Health Organization (WHO). WHO recommendations for the prevention of postpartum haemorrhage. Geneva, Switzerland: World Health Organization (WHO); 2007. 116 p.

Guideline Availability

Electronic copies: Available from the World Health Organization Web site .

Print copies: Available from the WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland; Phone: +41 22 791 3264; Fax: +41 22 791 4857; E-mail: bookorders@who.int.

Availability of Companion Documents

The following are available:

- WHO recommendations for preventing and treating PPH: evidence base. Geneva (Switzerland): World Health Organization (WHO); 2012. 48 p. Electronic copies: Available in Portable Document Format (PDF) from the World Health Organization (WHO) Web site .
- World Health Organization. WHO Handbook for guideline development. Geneva (Switzerland): World Health Organization (WHO); 2012. 63 p. Electronic copies: Available in PDF from the WHO Web site .

In addition, a process indicator can be found in section 6 of the original guideline document .

Patient Resources

None available

NGC Status

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